THE COMPLEMENTARY STRUCTURE OF DNA

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This paper reviews very briefly the recent work on the "structure" of the sodium salt of desoxyribonucleic acid (DNA). By structure is meant not the chemical formula but the spacial arrangement of the atoms. The structure revealed by X-rays is the general structure—that is, the features common to DNA from different sources, since the X-rays only respond clearly to the repeating part of the structure and effectively say nothing about the exact sequence of the bases, which probably does not repeat.

The general chemical formula has been described in these Proceedings by Professor A. R. Todd[1] and will be taken as known. The X-ray work is carried out on fibers drawn from extracted DNA from a variety of sources. The early studies were by Astbury and Bell.[2] Almost all the recent work has been done at King's College, London, by Drs. Wilkins and Franklin and their colleagues. Preliminary studies are reported in Wilkins, Gosling, and Seeds.[3] More detailed reports on the X-ray data have been given in two papers by Franklin and Gosling.[4] Evidence for the helical nature of the structure and for some of its other features has been presented in a preliminary way by Wilkins, Stokes, and Wilson[5] and by Franklin and Gosling.[6] More detailed interpretations of the crystalline form have been given by Franklin and Gosling[7] and by Wilkins, Seeds, Stokes, and Wilson.[8] In addition, Wilkins and Randall[9] have shown that the oriented sperm heads give a very similar X-ray pattern to that from extracted DNA.

The interpretation of their results offered by the experimentalists is in broad agreement with the type of structure proposed by Watson and Crick,[10] though the precise dimensions of this model may be incorrect. A more detailed description of the proposed structure and an account of the methods used in arriving at it have been given by Crick and Watson.[11] As is well known, this structure consists of two helical phosphate-sugar chains, winding round the same axis, the chains running in opposite directions. The chains are linked together by hydrogen bonds between their bases, a base from one chain being paired off with the opposite base on the other chain.

It is postulated that specific pairing occurs and that the only pairs that will normally fit into the structure are

adenine with thymine,
guanine with cytosine (or its derivatives).

The model places no restriction on the sequence of bases along a single chain. If the sequence of the bases on one chain were known, the sequence on the other chain could be written down because of the specified pairing. Thus each chain, with its bases, can be regarded as the "complement" of the other.

The salient features of this structure are as follows:

a) There are two chains in the structural unit.[12] This is strongly suggested by the observed density (which rules out three chains). Model-building shows that a single-chain structure is unlikely. The X-ray data also show "two-ishness."

b) The chains are arranged helically. This was originally postulated as the obvious way to explain the large dimensions of the unit cell. It has now received overwhelming support from the detailed X-ray data, interpreted in the light of the helical diffraction theory of Cochran, Crick, and Vand[13] (also Stokes, unpublished).

c) The chains are held together by specific pairs of bases. It is not generally realized that this feature was not assumed originally in the model-building but was introduced as the only way of joining the two chains together which was structurally plausible. Moreover, it has been shown by Watson and Donohue (unpublished) that, of all the possible ways of forming specific sets of pairs of bases, only two sets give symmetrical relationships to the glycosidic bonds. One of these sets satisfies the requirements only very poorly, and a suitable structure cannot be built using it. The other is the specific pairing incorporated in the proposed structure. Thus, even if no analytical data had been available, a sufficiently self-confident model-builder could have arrived at the correct specific pairing. Naturally, the knowledge of the observed base ratios made this step easier to take.

As is well known, the present analytical data give very strong support to this pairing, since, as was first pointed out some time ago by Chargaff,[14] the amount of adenine is found to be practically the same as the amount of thymine, and the amount of guanine the same as that of cytosine, for all sources of DNA so far studied, although the adenine/guanine ratio can vary considerably from one source to another. The most recent analytical evidence[15] shows that the base ratios expected to be 1:1 are indeed very close to this.

The hydrogen-bonding of the bases is also supported by physical-chemical data, but this will not be reviewed here.

It should be clearly realized that the specific pairing of the bases is the direct result of the regular helical nature of the backbone. Without this regularity, many different pairs of bases could be formed. Thus we can now see that the helical diffraction pattern and the analytical data are both reflections of the same thing—namely, the regularity of the phosphate-sugar backbone.

The DNA fibers exist in two forms—the crystalline (A) and the so-called "paracrystalline" (B), depending on the humidity. The structure proposed by Watson and Crick was for the B form, but any proof of the structure must come from A, as this gives much better pictures. The complete interpretation of these extremely beautiful X-ray photos by the King's College workers is eagerly awaited. Until this has been accomplished, no structure can be regarded as completely proved.

It is worth noting that, since the structure is sprinkled with diads (strictly, pseudo-diads) perpendicular to the fiber axis, the phase determination more closely corresponds in difficulty to that for a structure with a center of symmetry. If it were not for this (since a true center of symmetry is impossible because of the asymmetric atoms of the backbone), the correct structure would be much more difficult to establish.

Note that there is, as yet, no *direct* evidence as to whether the helices are right-handed or left-handed (or, less likely, a mixture of both). The proposed model is right-handed. The model-builders were unable to construct a satisfactory left-handed model, but this may merely reflect a lack of ingenuity on their part. Some direct evidence on this point would be most desirable.

Finally, it is highly unlikely that the structure is an "artifact" produced by the extraction process, since similar X-ray patterns have been obtained from intact biological material, such as oriented sperm heads (Wilkins and Randall[9]) and bacteriophage.[5]

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[1] A. R. Todd, these PROCEEDINGS, **40**, 752–759, 1954.

[2] W. T. Astbury and F. O. Bell, *Nature*, **141**, 747, 1938; W. T. Astbury in *Nucleic Acid, Symposia Soc. Exptl. Biol.*, **1**, 66, 1947.

[3] M. H. F. Wilkins, R. G. Gosling, and W. E. Seeds, *Nature*, **167**, 759, 1951.

[4] R. F. Franklin and R. G. Gosling, *Acta Cryst.*, **6**, 673, 1953; *ibid.*, **6**, 678, 1953.

[5] M. H. F. Wilkins, A. R. Stokes, and H. R. Wilson, *Nature*, **171**, 738, 1953.

[6] R. E. Franklin and R. G. Gosling, *Nature*, **171**, 740, 1953.

[7] R. E. Franklin and R. G. Gosling, *ibid.*, **172**, 156, 1953.

[8] M. H. F. Wilkins, W. E. Seeds, A. R. Stokes, and H. R. Wilson, *ibid.*, **172**, 759, 1953.

[9] M. H. F. Wilkins and J. T. Randall, *Biochim. et Biophys. Acta*, **10**, 192, 1953.

[10] J. D. Watson and F. H. C. Crick, *Nature*, **171**, 737, 1953.

[11] F. H. C. Crick and J. D. Watson, *Proc. Roy. Soc. London, A*, **223**, 80, 1954.

[12] This in no way conflicts with the recent suggestion of Schachman and Dekker that there are occasional random breaks in the phosphate-sugar backbone. The X-rays see clearly only the idealized, repeating pattern.

[13] W. Cochran, F. H. C. Crick, and V. Vand, *Acta Cryst.*, **5**, 581, 1952.

[14] E. Chargaff, *Experientia*, **6**, 201, 1950.

[15] See, for example, G. R. Wyatt, in V. T. Bowen, *The Chemistry and Physiology of the Nucleus* (New York: Academic Press, 1952), p. 201; E. Chargaff and R. Lipshitz, *J. Am. Chem. Soc.*, **75**, 3658, 1953.